THE UNIVERSITY OF MICHIGAN DIOXIN EXPOSURE STUDY OUTLIER INVESTIGATIONS: MAIN RESULTS AND LESSONS LEARNED

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Introduction

The University of Michigan Dioxin Exposure Study (UMDES) was motivated because of concerns about possible human exposure to dioxins discharged as a result of historical industrial activities of the Dow Chemical Company located in Midland, Michigan, USA. A number of investigations have documented widespread dioxin contamination of soils in Midland downwind of incineration activities at Dow (i.e., the plume area), and in the flood plain and river sediments of the Tittabawassee River and further downstream from the Dow plant [1,2]. The congener profiles of dioxin contamination in these two areas differ, with contamination in the plume area dominated by polychlorinated dibenzo-*p*-dioxins (PCDDs), and contamination in the flood plain of the Tittabawassee River dominated by two polychlorinated dibenzofurans (PCDFs), 2,3,7,8-TCDF and 2,3,4,7,8-PeCDF [1]. The main focus of the UMDES has been to identify and quantify potential pathways of human exposure to dioxins in the contaminated areas.

The was a large, carefully planned and executed, population-based exposure pathway study that involved cutting-edge survey methodologies, careful sample collection (blood, household dust, and soil) and state-of-the art analytical chemistry [3]. Field data collection was largely completed in 2004-2005, initial results became available in 2006, and main results were published in 2009 [4,5,6]. The models presented in these papers summarize results as they pertain to various segments of the study population. So, for example, linear regression models primarily describe mean effects, and logistic models describe associations at a specified quantile, such as the 95th percentile of the study population. Such models can be very useful for understanding major trends and associations in the data, but they do not necessarily reflect important pathways of exposure among the few study participants with the very highest levels of dioxins in blood, dust and/or soil, so-called outliers.

While the right-skewed nature of the distributions of dioxin levels in blood, dust and soil are not necessarily new or surprising, this is one of the few large general population studies of dioxins that has involved follow-up investigations of study participants with 'high' or 'outlier' results for blood, dust or soil in an attempt to understand what factors may be associated with 'outlier' status. This report summarizes main results of outlier investigations of blood, household dust and soil, and lessons learned.

Materials and Methods

The main UMDES involved a two-stage clustered random sampling design to recruit subjects from five regions in the State of Michigan, USA. The regions were: the 100-year Federal Emergency Management Agency (FEMA) floodplain of the Tittabawassee River or whether the respondent reported flooding of the home by the Tittabawassee River (FP); the near-floodplain of the Tittabawassee River (NFP); the plume area in the City of Midland downwind from the historic incineration activities of the Dow plant (PL); elsewhere in Midland and Saginaw counties and parts of Bay County outside of the floodplain, near-floodplain and plume areas (MS); and Jackson and Calhoun Counties (located more than 200 kilometers away from the Dow facilities in Midland) that served as a control area (JC). Eligible subjects were required to be at least 18 years old and to have lived in their homes for at least 5 years. Data

collection for the main study involved an hour-long interview and obtaining blood, household dust, and soil samples for chemical analyses from eligible subjects. Overall, 946 subjects provided blood samples that were analyzed for the WHO 29 PCDDs, PCDFs and PCBs by Vista Analytical Laboratory (El Dorado Hills, California) using modified United States Environmental Protection Agency methods 8290 and 1668, Revision A [7,8]. Serum results are reported in parts per trillion (ppt) on a lipid adjusted basis; soil and dust results are reported in ppt on a dry weight basis. TEQ values are calculated using 2005 TEFs [9]. Full details of methods for the parent study are available elsewhere [1,3].

After the field data collection for the main UMDES study was completed and initial results became available, it was decided to initiate a number of follow-up investigations of 'outliers', i.e., subjects with high levels of dioxins in blood, dust or soil. A number of outlier investigations were completed and four are summarized here: 1) the individual with the highest serum TEQ in the study (TEQ=211 ppt); 2) the person who had the highest serum 2,3,4,7,8-PeCDF level (after adjustment for age and body mass index (BMI)); 3) the 20 study participants with the highest TEQ levels in house dust; and 4) study participants who had the highest soil TEQ levels among those who lived outside of areas of known contamination (i.e., outside of the plume and the flood plain) [10,11,12,13]. Follow-up investigations involved more extensive, open-ended interviews with the involved study participants, in addition to other approaches. Statistical analyses were performed using SAS version 9.1 and STATA version 10 [14,15].

Results and Discussion

Each of the outlier investigations is summarized below.

Human Exposure to Dioxins from Clay [10]: For the general population, the dominant source of exposure to dioxin-like compounds is food. The total serum TEQ from the index case was 211 ppt on a lipid-adjusted basis, which was the highest value observed in the UMDES study population (overall mean TEQ = 21.3 ppt in the control population). This subject had no apparent opportunity for exposure to dioxins, except that she had lived on property with soil contaminated with dioxins for almost 30 years, and had been a ceramics hobbyist for more than 30 years. Soil from her property and clay that she used for ceramics were both contaminated with dioxins, but the congener patterns differed. The congener patterns in this subject's serum, soil, and ceramic clay suggested strongly that the dioxin contamination in clay, and not the soil, was the dominant source of dioxin contamination in her serum. Two of her friends who were also long-term ceramics enthusiasts also were studied and had a similar pattern of dioxins in their serum. It appears that working with ceramic clay (particularly ball clay), whether directly handling clay and/or the process of firing clay with unvented kilns, can be a significant non-food and non-industrial source of human exposure to dioxins among ceramics hobbyists. The extent of human exposure from ceramic clay is unclear, but it may be widespread. This is the first report that documents human exposure to dioxins in clay.

Eating beef from cattle raised in the flood plain of the Tittabawassee River [11]: As noted above, most of the toxic equivalency in Tittabawassee River sediments is from two furan congeners, 2,3,7,8-TCDF and 2,3,4,7,8-pentaCDF. The individual with the highest adjusted (for age, age^2, and body mass index) serum level of 2,3,4,7,8-pentaCDF in the study (42.5 parts per trillion) reported a unique history of raising cattle and vegetables in the flood plain of the Tittabawassee River. Interviews and serum samples were obtained from the index case and 15 other people who ate beef and vegetables raised by the index case. 2,3,4,7,8-pentaCDF in beef lipid was estimated to have been more than three orders of magnitude greater than background (1,780 versus 1.1 parts per trillion). The mean, median, and 95th percentile for serum 2,3,4,7,8-pentaCDF in the study control population were 6.0, 5.4, and 13.0 parts per trillion, respectively, and were 9.9, 8.4, and 20.5 parts per trillion among beef/vegetable consumers, respectively. Back extrapolation for the index case suggests that his increase in serum concentration of 2,3,4,7,8-pentaCDF over background may have been as high as 146 parts per trillion. Consumption of beef and/or vegetables raised on dioxin-contaminated soil may be an important completed pathway of exposure. An important public health message is that animals and crops should not be raised for human consumption in areas contaminated with dioxins.

Investigations of household dust outliers [12]: As part of the University of Michigan Dioxin Exposure Study, the 29 congeners of PCDDs, PCDFs, and dioxin-like PCBs that have World Health Organization consensus toxic equivalency factors were measured in house dust from 764 homes using a population-based sampling design over selected regions in five Michigan counties. Twenty homes had a total toxic equivalency in house dust that was more than 2.5 standard deviations above the mean (i.e., defined to be outliers). The congener distributions in the house dust outliers varied and were dominated (i.e., >50% of the total TEQ) by either polychlorinated dibenzo-p-dioxins (n = 9), polychlorinated dibenzofurans (n = 1), or dioxin-like polychlorinated biphenyls (n = 9). Likely sources of contamination of house dust were positively identified in only three cases. In two cases, dust contamination appeared to be related to contaminated soil adjacent to the home; in one case, contamination was related to a source within the home (a carpet pad). In most cases, the precise source(s) of contamination of house dust could not be identified but appeared likely to be related to uncharacterized sources within the homes, rather than outside the homes.

Investigation of residences with anomalous soil concentrations of dioxin-like compounds [13]: Most contamination of residential property soil with dioxin-like compounds occurs as a result of proximity to industrial activity that produces such compounds and, outside the industrially impacted zone, the soil concentrations are assumed to be at background levels. However, as part of the University of Michigan Dioxin Exposure Study, residential properties in the lower peninsula of Michigan, USA, were identified that were located far enough from known sources of these compounds that the soil concentrations should have been at background levels and yet the TEQ of some properties' soil was greater than 2.5 standard deviations above the mean background level. In the cases presented from Midland/Saginaw Counties, the anomalously high-TEQ values were primarily due to the presence of polychlorinated dibenzofurans. Based on interviews with the residents and a comparison of soil congener profiles, it was deduced that these values resulted from anthropogenic soil movement from historically contaminated areas. For example, soil and/or mulch was taken from the flood plain to be used in a garden, or soil from the flood plain was used as fill to level residential properties. In the cases from Jackson/Calhoun Counties, the unusually high TEQ values were primarily due to polychlorinated biphenyls. In one profiled case, it appeared that the study participant's residential soil became contaminated through sandblasting to remove paint from a backyard swimming pool. This study identified two mechanisms for soil contamination outside zones of industrial impact. The assumption of background levels of soil contamination outside industrial zones may not be valid. More generally, it was estimated that 23% (95% CI: 15.4% – 30.6%) of residential properties outside of the floodplain but within 8 km of the floodplain showed evidence of contamination consistent with soil coming from the floodplain, most likely through the anthropogenic movement of contaminated soil or other materials.

Overall, the outlier investigations identified a number of unanticipated and/or novel hypotheses: 1) ceramic clay can be an important source of human exposure to dioxins among ceramicists; 2) raising animals for human consumption on contaminated soil can result in a completed pathway of exposure to dioxins in soil; 3) very high levels of dioxins in household dust more often appear to be the result of uncharacterized emission sources within homes, rather than external contamination intruding into homes; and 4) anthropogenic movement of soil may be common and can result in substantial spread of contamination outside of zones of initial industrial contamination.

Aside from being part of the main UMDES, these outlier investigations share an important feature: new information leading to novel hypotheses was largely based on open-ended follow-up interviews with study participants. Clearly, all of these investigations were made possible by the complex study design of the UMDES, but it is important to remember that relatively simple tools, such as open-ended interviews, can yield valuable and interesting results.

Acknowledgments
Financial support for this study comes from the Dow Chemical Company through an unrestricted grant to the University of Michigan. The authors acknowledge Dr. Donald Patterson Jr., and Ms. Sharyn Vantine for their assistance, and Drs. Linda Birnbaum, Ronald Hites, Paolo Boffetta, and Marie Haring Sweeney for their guidance as members of our Scientific Advisory Board.

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